REMARKS/ARGUMENTS

Claims 1-11 were pending. The present Response amends claims 1-4, and 9-11. Support for the amendment to claims 1 and 2, and claims depending therefrom, directed to a molecule selected from the group consisting of a glucagon-like peptide-1, a biologically active fragment, variant, analog, mimetic, agonist or derivative thereof, and an exendin can be found at least at page 8, lines 1-3; and page 16, lines 1-3. Support for the amendments to the specification can be found at least at page 1, the text under the heading "FIELD OF THE INVENTION"; page 1, lines 14-25; page 1, line 31, to page 2, line 31 of the parent application USSN 09/953,021. Applicants have incorporated this language by reference into the present application to provide support that a method directed to ameliorating, treating or preventing skeletal tissue injury finds support in the parent application, and this claim is, therefore, entitled to claim priority back to the parent application. Applicants submit that no new matter is introduced thereby.

Specification/Claim/Objections

The Patent Office has raised two objections to the application: in page 11, line 3, "SEQ ID NO 3" should be changed to "SEQ ID NO:3" and in claims 1 and 9, spell out "GLP-1" and "PVD," respectively. The instant amendments obviate the Patent Office's objections.

Issues under 35 U.S.C. 112, second paragraph

The Patent Office has rejected claims 1-11 under 35 U.S.C. §112, second paragraph for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, the Patent Office cites claim 1 as reciting "treating or preventing." The Patent Office alleges that the recitation is unclear as to which process the claimed method is directed, treating or preventing. Applicants respectfully submit that there is no ambiguity in the scope of the claim. The term "or" has been found by the Patent Office to be an acceptable form of an alternative expression (MPEP 2173.05(h)). Applicants submit that the scope of the claims

directed to (a) "a method of treating intermittent claudication in a subject comprising the step of administering a therapeutically effective amount of GLP-1 molecule" and (b) "a method of preventing intermittent claudication in a subject comprising the step of administering a therapeutically effective amount of GLP-1 molecule" are definite and clear. Accordingly, the scope of a claim directed to "a method of treating or preventing intermittent claudication in a subject comprising the step of administering a therapeutically effective amount of GLP-1 molecule" is also definite and clear (*i.e.*, the scope encompasses the metes and bounds of claims (a) and (b)). Similarly, claim 2 is also not indefinite. Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1 and 2 and claims dependent therefrom.

In claim 3, the Patent Office alleges that it is not clear whether or not "GLP-1 (7-36)NH_2" refers to amine group(s) of any lysine side change(s) or carboxyl terminal amide group. Applicants have amended claim 3 to include (SEQ ID NO:4) to obviate this rejection. The Patent Office also alleges that the recitation of "the GLP-1 molecule..., and exendin-4" is also unclear. Applicants have replaced the phrase "GLP-1 molecule" to obviate this rejection. The Patent Office further alleges that claim 3 lacks antecedent basis for the limitation "the GLP-1 molecule." Applicants have amended claim 3 to obviate this rejection.

Applicants have amended claim 4 in keeping with the amendments of claim 3 to obviate the rejection.

The Patent Office also notes that claim 3 is indefinite in the use of "GLP-4 (7-37)." Applicants have amended claim 3 to obviate this rejection.

In claim 11, the Patent Office alleges that the term "formulation" is indefinite because the claim does not make it clear as to whether or not said formulation comprises the GLP-1 peptide. Applicants have amended the claim to obviate this rejection.

Issues Under 35 U.S.C. §112, first paragraph

The Patent Office has rejected claims 1-11 under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Patent Office alleges that the specification fails to provide sufficient description regarding how to use GLP-1 or analog thereof, or exendin-4 for treating intermittent claudication that is caused by or associated with atherosclerosis-related peripheral vascular disease. Applicants submit that a description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption (MPEP 2163.04). The examiner must present by a preponderance of the evidence why a person of skill in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims.

Applicants submit that one of ordinary skill in the art would be familiar with how to use (administer) GLP-1, or analogs thereof, or exendins, as they are the subject of much research (a quick pubmed search on the National Institute of Health website resulted in over 1400 entries). Moreover, Applicants submit that the specification provides enough information and reasoning for one of ordinary skill in the art to reasonably conclude that Applicants had possession of the claimed invention, see for example, page 3, line 6, to page 6, line 9, where a description of the problem is provided, and page 9, line 16, to page 10, line 19 as well as page 20, lines 1-29, where a solution and the reasoning behind the invention is provided. The Patent Office, having provided no evidence or reasoning to contradict the teaching of the specification, has not established its burden in order to reject the application based upon insufficient description.

In general, it should also be noted that compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed (MPEP 2164.02). However, in this case, Applicants submit that the application describes the effect of GLP-1 on

cardiac muscle ischemia and reperfusion in rats and dogs. Through these experiments, Applicants have provided evidence that their reasoning is sound, further supporting the reasonableness of the invention to the skilled artisan.

The Patent Office alleges that the Applicants were not in possession of a method of preventing IC disorder state that is caused by or associated with PVD. Applicants respectfully disagree. IC is defined as lower extremity pain, muscle ache or muscle fatigue usually precipitated by exertion. IC results from ischemic disease of skeletal muscle characterized by repeated bouts of ischemia-reperfusion (page 2, lines 18-24 of the application). Applicants' invention is directed to treating (ameliorating) or preventing the injury to skeletal tissue caused by ischemia-reperfusion. Thus, by ameliorating or preventing the ischemic-reperfusion injury to skeletal tissue, IC itself may be prevented. Applicants submit that, based upon the teachings in the specification, one of ordinary skill in the art could reasonably conclude that Applicants had possession of the invention.

The Patent Office alleges that the application discloses only the method of GLP-1 treatment for cardiac muscle ischemia disorder state but not a method of GLP-1 treatment or prophylaxis of IC disorder state that is caused by or associated with PVD. Applicants respectfully disagree. The examples using cardiac muscle merely exemplify the broader teachings of the application relating to ischemia-reperfusion injury to tissues and how they can be ameliorated/prevented by GLP-1, a biologically active fragment, variant, analog, or derivative thereof, or an exendin. Applicants have provided sufficient information for the skilled artisan to understand the metes and bounds of the invention, the amelioration/treatment or prevention of skeletal muscle injury due to ischemia-reperfusion. By ameliorating or preventing the ischemia-reperfusion induced skeletal muscle injury, IC can be ameliorated or prevented. Applicants submit that they have provided scientific reasoning, with examples that confirm aspects of their teaching, which are more than a mere statement that it is part of the invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection to the claims as amended.

CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and request that a timely Notice of Allowance be issued in this case. The Examiner is encouraged to call the undersigned attorney to discuss any issues related to the prosecution of the instant application.

Applicants believe that no additional fee is necessitated by the present paper. However, in the event any fees are due or any amount is to be credited as a result of the present Response, Applicants authorize the Commissioner of Patents to debit or credit Deposit Account No. 010535.

Respectfully submitted,

6/28/2004

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